PATENT APPLICATION SAH #S 3-10-00

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Stephen Peter FITZGERALD et al.

Application No.: 09/389,082

Filed: September 2, 1999

Group Art Unit: 1743

Handy

Docket No.: 104161

For: IMPROVEMENTS RELATING TO ASSAY DEVICES

CLAIM FOR PRIORITY

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The benefit of the filing date of the following prior foreign application filed in the following foreign country is hereby requested for the above-identified patent application and the priority provided in 35 U.S.C. §119 is hereby claimed:

European Patent Application No. 98307732.2 filed September 23, 1999

In support of this claim, a certified copy of said original foreign application:

__X__ is filed herewith.

_____ was filed on _____ in Parent Application No. _____ filed _____.

It is requested that the file of this application be marked to indicate that the requirements of 35 U.S.C. §119 have been fulfilled and that the Patent and Trademark Office kindly acknowledge receipt of this document.

Respectfully submitted,

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Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. | Patent application No. | Demande de brevet n°

98307732.2

Der Präsident des Europäischen Patentamts;
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets
p.o.

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Blatt 2 der Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

Anmeldung Nr.:
Application no.: 98307732.2
Demande n°:

Anmeldetag:
Date of filing: 23/09/98
Date de dépôt:

Anmelder:
Applicant(s):
Demandeur(s):
Randox Laboratories Ltd.
Crumlin, Co. Antrim BT29 4QY
UNITED KINGDOM

Bezeichnung der Erfindung:
Title of the invention:
Titre de l'invention:
Multi-well plate with immobilized-reagent matrix on biochip inserted into each well

In Anspruch genommene Priorität(en) / Priority(ies) claimed / Priorité(s) revendiquée(s)

Staat:	Tag:	Aktenzeichen:
State:	Date:	File no.
Pays:	Date:	Numéro de dépôt:

Internationale Patentklassifikation:
International Patent classification:
Classification internationale des brevets:
B01L3/00, // C12M1/40, G01N33/53

Am Anmeldetag benannte Vertragstaaten:
Contracting states designated at date of filing: AT/BE/CH/CY/DE/DK/ES/FI/FR/GB/GR/IE/IT/LI/LU/MC/NL/PT/SE
Etats contractants désignés lors du depôt:

Bemerkungen:
Remarks:
Remarques:

The original title of the application reads as follows:
Improvements relating to assay devices

The invention relates to assay devices for immunoassays and the like.

Recently, in order to increase the throughput of immunoassays, assay devices in the form of chips have been developed on which is deposited an array of localised reactive sites containing potentially many different reactive species, for example different antibodies. These reactive species react with a respective different analyte in a sample supplied to the chip. Following removal of the unbonded sample, the chip can then be examined to determine the presence or absence of the respective analytes. An example of a method for preparing the reaction sites is described in more detail in our co-pending European Patent Application No. 97302707.1 and a method for analysing the substrate is described in more detail in our co-pending European Patent Application No. 97307053.5. Both applications are incorporated herein by reference. The analysis typically involves viewing and measuring chemiluminescent radiation at the reaction sites using a low light level CCD camera system or the like.

A problem with these substrates is that they are small having typical dimensions 10mm x 10mm x 1mm thus making them difficult to handle. This problem is enhanced by the fact that the chips carry many small reaction sites which will be damaged if incorrectly handled. A typical chip will have 100 or more such reaction sites.

In accordance with a first aspect of the present invention, we provide a method of preparing an assay assembly, the method comprising placing an assay device in a storage well having a base and sidewall. The method preferably further comprises providing a protective, removable packaging over the storage well.

In accordance with a second aspect of the present invention, an assay assembly comprises an assay device located in a storage well having a base and sidewall. A

protective, removable packaging may be provided over the storage well for protecting the assay device in transit.

We also provide a storage well for such an assembly.

This invention overcomes the problems mentioned above by placing the assay device in a storage well, thus protecting the assay device while it is being handled during an immunoassay process. In addition, by providing a protective, removable packaging over the storage well, the complete assembly of assay device, storage well, and packaging can be prepared centrally and then sent to the end user easily and without risk of damaging the assay device and in particular the reactive sites. The form of the storage well will depend on a number of factors. If, for example, the reactive sites are to be examined using a chemiluminescent (or fluorescent or other lighting machine) technique, it is advantageous to make the walls of the storage well dark, preferably black, to reduce reflections/scattering of light and, where the storage well is joined to adjacent storage wells, to reduce or eliminate the transmission of light into adjacent wells. The base and sidewall of the storage well may therefore be made of a black material such as pigmented plastic or could be coated/painted in a black material.

The base is preferably continuous but could have a central aperture surrounded by a lip.

Another problem which can arise with the use of storage wells is due to the liquid meniscus of the liquid reagent which is used in the storage well during the immunoassay. If this reagent must remain in the well during a final analysis stage, the meniscus will contribute to distortion and abberation of the image of the reactive sites viewed by the camera system.

One approach is to place the assay device on its edge in the storage well. The well would then need to have a transparent side wall to enable the reactive sites to be viewed or could have a sufficiently large top opening to enable the device to be viewed from the top.

Conventionally, however, the inner surface of the sidewall tapers inwardly adjacent the base. The use of a tapering sidewall allows the cross-sectional area of the open part of a well to be maximised and therefore that of the meniscus which is thereby flattened and thus the abberations are reduced. Also, the assay device can be laid flat on the base for viewing from the top.

Further flattening can be achieved by the selection of suitable well material and internal surface finish. Of course, the material chosen for the wells and any coatings applied to the inside should be chemically unreactive so as not to effect the immunoassay. Preferred materials comprise PVC and polypropylene.

A further advantage of the use of a taper is that it facilitates easy substrate placement and location. This is particularly important in the case of an automated process for loading substrates into the wells.

Although individual storage wells could be provided, preferably a number of such storage wells are provided fixed together in an array. This again simplifies the handling of assay devices by protecting them within the wells and also makes it easier to handle the storage wells since the array will have a larger size than each individual well.

Preferably, the assay device is retained in the storage well by some form of retaining means. The retaining means could be in the form of retaining clips or adhesives to glue the substrates to the base. Neither of these is particularly desirable since they could effect the immunoassay. Preferably, the retaining means comprises one or more hot or cold formed projections on the inner surface of the sidewall. These could be formed prior to supplying the substrate, which is then press fitted into the well, or after the substrate has been supplied.

Typically, each storage well is square in plan since this is suited to the square format of conventional CCD

cameras. However, other plan forms such as rectangular or circular are envisaged.

To further ease handling, preferably the assembly further comprises a carrying tray for carrying one or more storage wells for use with an assay device processing instrument.

Such a carrying tray can then be used not only for holding the storage well(s) during supply to a user but also in an immunoassay machine.

An example of an array of storage wells according to the invention will now be described with reference to the accompanying drawings, in which:-

Figure 1 is a perspective view of the array from above;

Figure 2 is a section taken on the line 2-2 in Figure 1 but showing a biochip in one of the storage wells;

Figure 3 is a perspective view of the section shown in Figure 2; and,

Figure 4 is a perspective view of a carrying tray for the array of storage wells.

Figure 1 illustrates an array of three storage wells 1-3 formed from a one-piece plastics moulding of P.V.C. or polypropylene. For the reasons given above, the plastics material incorporates a black pigment. Each storage well 1-3 has a similar form and as can be seen in Figure 1 is substantially square in plan. For convenience, only the storage well 1 will be described in detail.

The storage well 1 has a base 4 and a sidewall 5 surrounding the base. As can be seen in Figure 2, the sidewalls 5 of each storage well are integrally formed at the junctions between the storage wells.

Protrusions 6 are moulded at each end of the array to enable the array to be handled easily.

Each sidewall 5 has an upper section 7 which is substantially vertical with respect to the base 4 and a lower section 8 which tapers inwardly. The taper terminates just short of the base 4 so as to define a

region 9 having a width and height corresponding to that of a biochip 10. Typical array dimensions are: 42mm long, 9mm high and 14mm wide at the top.

Following construction of the array of storage wells 1-3, each is supplied with a biochip 10. The biochips 10 are prepared in a conventional manner by immobilising ligands on respective reaction sites by means of microfluidic dispensing of the ligand onto the substrate, which is chemically activated. Covalent immobilisation is necessary to ensure ligands are not released during incubation and washing steps. Each chip which has dimensions 10mm x10mm and is about 1mm thick is then dropped into the respective storage well 1-3 and one such biochip 10 is shown in the storage well 1 in Figures 2 and 3.

Each biochip 10 is then secured in the base of the storage well by cold or hot forming bumps 11 on at least one side section of the sidewall 5. These bumps may be either preformed for press fitting or post-formed after insertion of the biochip 10.

As well as being tapered, the inner surfaces of the sidewalls 5 are preferably provided with a polished finish to reduce the curvature of the liquid meniscus and minimise optical abberations.

Following these steps, the set of three storage wells can then be prepacked in an individual sealed "bubble" on a tape forming a roll for reel dispensing. However, in the preferred approach, three sets of storage well arrays of the type shown in Figure 2 are loaded onto a carrying tray 20 as shown in Figure 4. This carrying tray is made of a plastics moulding and has two sets of crossbars 21,22 extending between opposite sidewalls 23,24 respectively. Nine openings 25 are defined into which the respective storage wells can be located. Each set of three storage wells 1-3 is loaded parallel to the crossbars 21 with the crossbars 22 entering into corresponding recesses 30 between adjacent storage wells. The loaded carrier tray is

then sealed in suitable packing materials for transportation. The user can then either remove the storage wells from the carrier tray or, preferably, leave them in place and use the carrier tray to move the storage wells about the immunoassay process.

CLAIMS

1. An assay assembly comprising an assay device located in a storage well having a base and side walls.

2. An assembly according to claim 1, further comprising a protective, removable packaging provided over the storage well.

3. An assembly according to claim 1 or claim 2, wherein the assay device comprises a chip on which an array of reactive species is immobilised.

4. An assembly according to any of the preceding claims, wherein the assay device substantially fills the area of the base.

5. An assembly according to any of the preceding claims, wherein the assay device is retained in the storage well by retaining means.

6. An assembly according to claim 5, wherein the retaining means comprises one or more hot or cold formed projections on the inner surface of the side wall.

7. An assembly according to any of the preceding claims, further comprising a carrying tray for carrying one or more storage wells for use with an assay device processing instrument.

8. A storage well for an assay assembly according to any of the preceding claims, the well having a base and side wall.

9. A well according to claim 8, wherein the inner surface of the side wall tapers inwardly adjacent the base.

10. A well according to claim 8 or claim 9, wherein the base is square.

11. A storage well according to any of claims 8 to 10, wherein the well comprises a plastics moulding.

12. A set of storage wells according to any of claims 8 to 11, the wells being fixed together in an array.

13. A set of storage wells according to claim 12, wherein an array comprises three storage wells, preferably arranged in a line.

14. A set of storage wells according to claim 12 or claim 13, when dependent on claim 11, wherein the wells in the array are made from a single plastics moulding.

15. A method of preparing an assay assembly, the method comprising placing an assay device in a storage well having a base and side wall.

16. A method according to claim 15, further comprising providing a protective, removable packaging over the storage well.

17. A method according to claim 15 or claim 16, further comprising securing the assay device in the storage well.

18. A method according to claim 17, wherein the securing step comprises hot or cold forming at least one projection on the inner surface of the side wall.

19. A method according to any of claims 15 to 18, wherein the storage well is in accordance with any of claims 8 to 14.

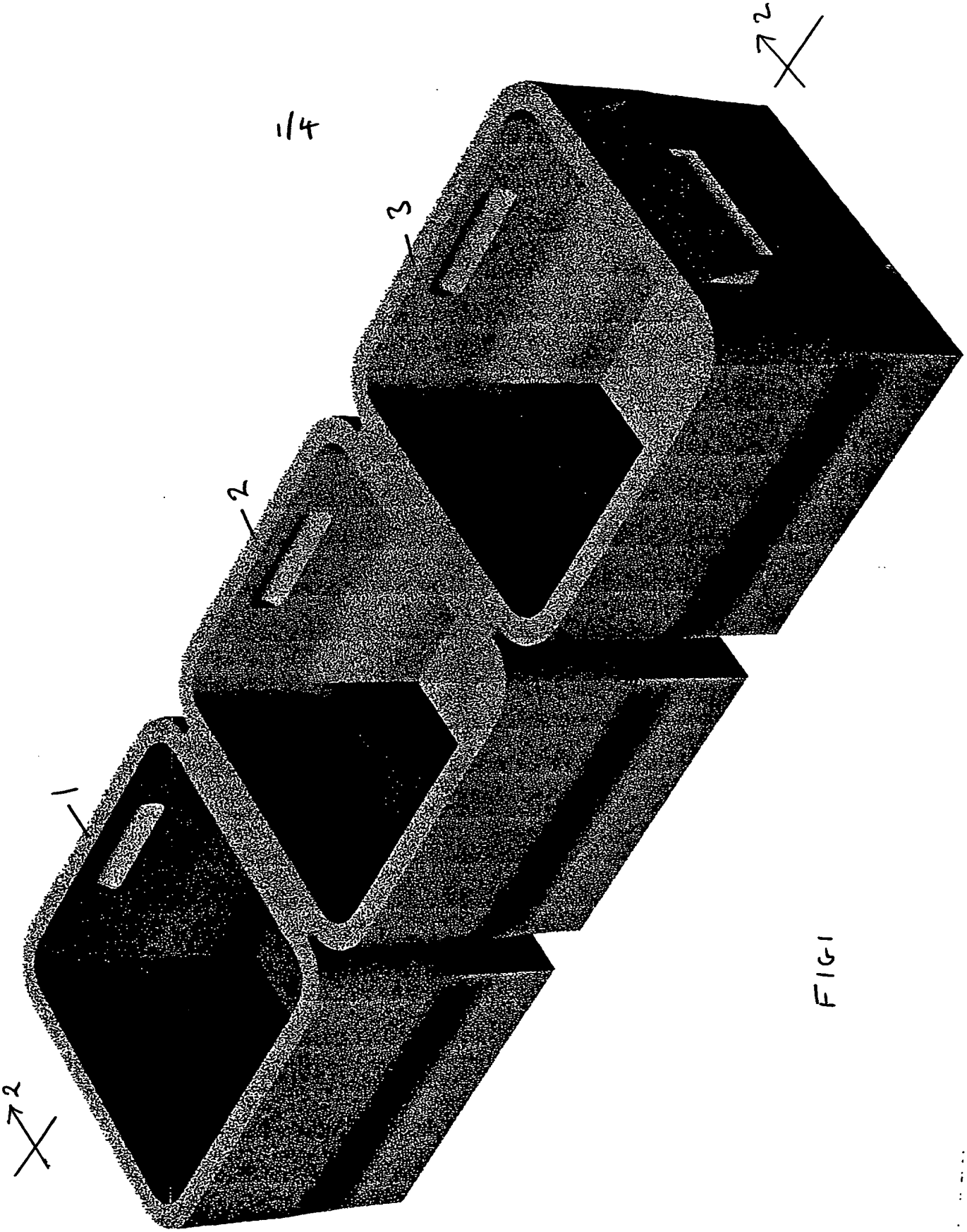

FIG1

2/4

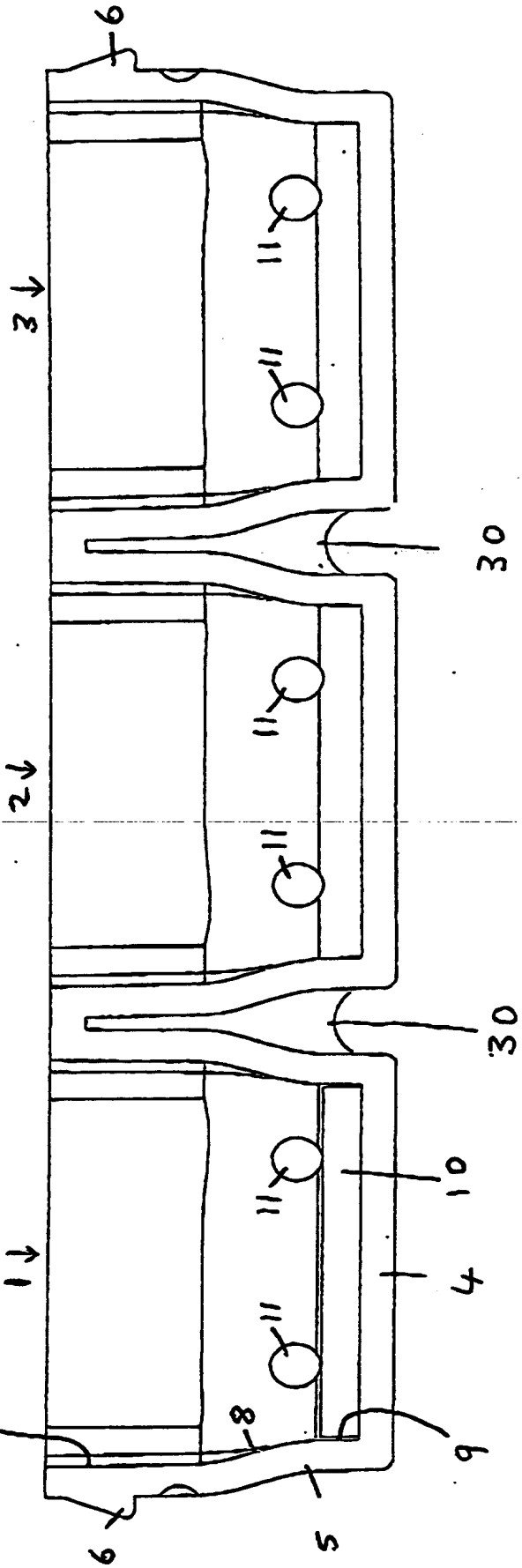

FIG 2

3/4

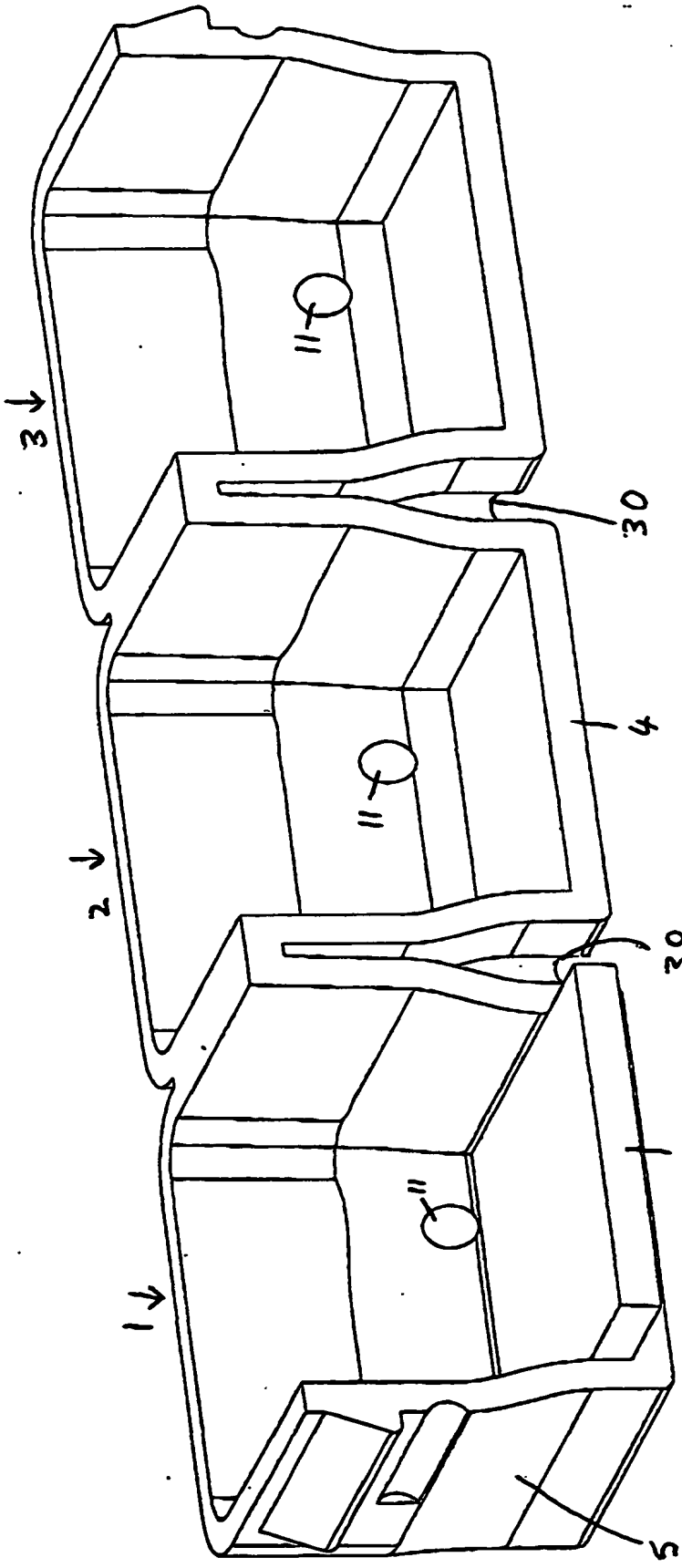

FIG 3

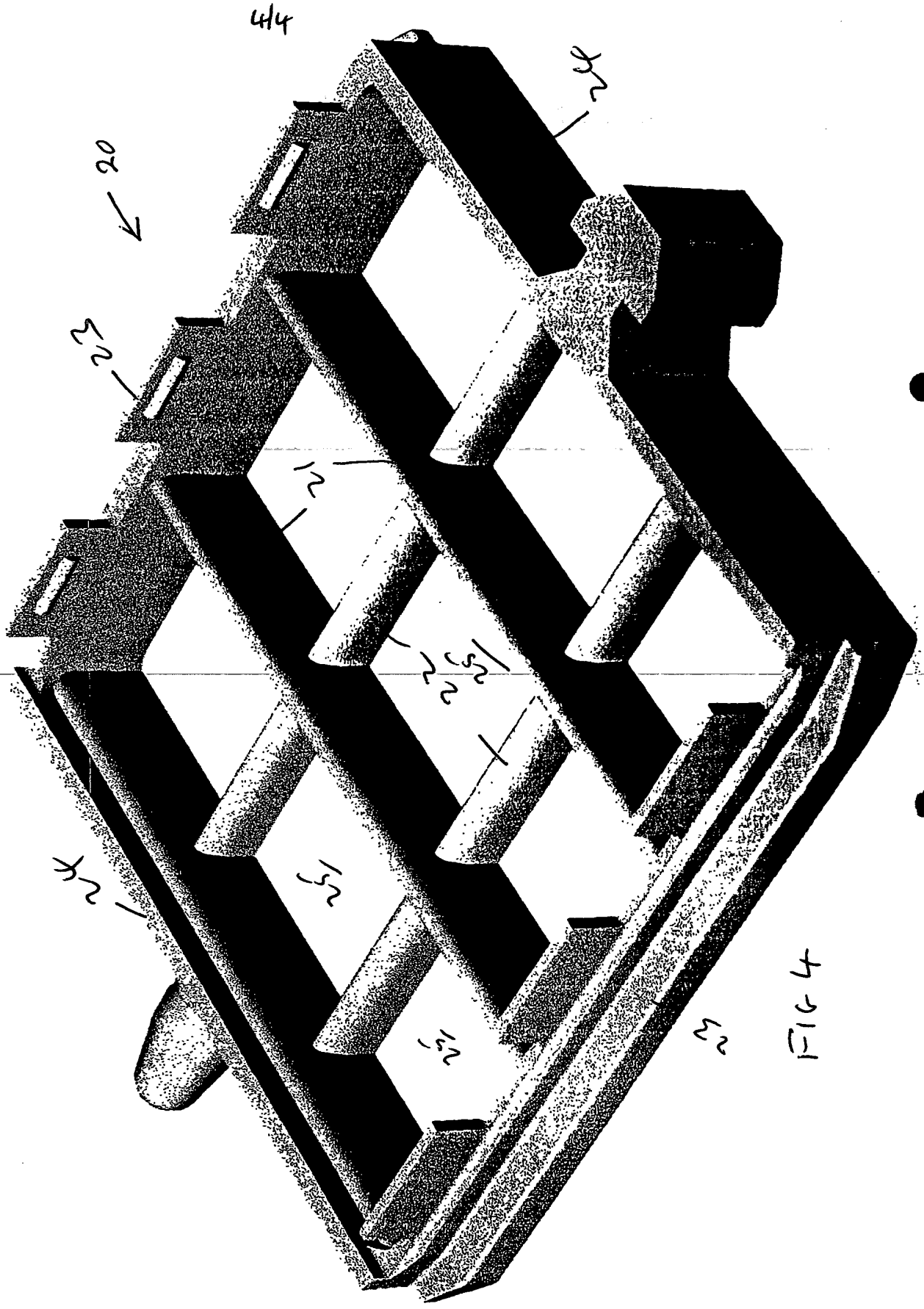

FIG 4

ABSTRACT

IMPROVEMENTS RELATING TO ASSAY DEVICES

An assay assembly comprising an assay device (10) located in a storage well (1-3) having a base (4) and side walls (5).